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In this issue we are pleased to present articles by Dr Barbara Lam, Dr Cheung Tak Cheong, Dr Hui Shiu Kei and Dr Kevin Loh.

All are senior clinicians with a lot to share in their respective specialties. I am sure you will derive much benefit from these informative yet easy to read articles.

With 3 years of experience behind us in running this Journal, we are confident to be able to improve the standard of the publication. We will continue to bring to you cutting-edge information in different areas in Internal Medicine. We hope you will also find the Journal useful in your daily practice.



Dr Lam Tat Chung, Paul

林達聰醫生

FRCP, FHKAM (Medicine),
FHKAM (Psychiatry)
President



Dr Lau Chu Pak

劉柱柏醫生

FRCP, MD, FHKAM (Medicine)
Chief Editor

Pictorial Medical History (1)

Dr Lam Tat Chung, Paul (林達聰醫生)

FRCP, FHKAM (Medicine), FHKAM (Psychiatry)

Specialist in Psychiatry, Private Practice Honorary Clinical Assistant Professor, University of Hong Kong

Traditionally the doctor's emblem contains a snake and rod design. There is some confusion about the origin of the sign. Some attributed it to the brazen snake created by Moses. According to the *Book of Numbers*, Moses led the Jews out of Egypt and wandered in the desert for 40 years before entering the Promised Land. During the journey, his followers encountered drought, plague and were bitten by snakes. The Lord instructed Moses to make a snake of bronze, and to mount it on a stick. Those inflicted by snakebite would be healed when they looked at it.

However, Moses, though a great prophet, had little connection with Medicine. The snake of Moses was not the origin of the doctor's emblem. (Note that the top of the rod is in the form of a T.)

The Brazen Snake by French painter Sebastian Bourdon (1653)



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Respiratory Syncytial Virus Bronchiolitis in Young Infants – Update on Management and Prevention



Dr Lam Cheung Cheung, Barbara, JP (藍章翔醫生、太平紳士)

*MBBS, MRCP(UK), FRCP(Edin., Lond.),
FRCPCH(UK), FHKAM(HK), FHKCPaed*

*Honorary Consultant,
Queen Mary Hospital,
Hong Kong Sanatorium & Hospital*

*Honorary Clinical Associate Professor,
Department of Paediatrics and Adolescent
Medicine,
University of Hong Kong*

Key words:

Respiratory syncytial virus (呼吸道合胞病毒), bronchiolitis (細支氣管炎), management (治理), prevention (預防)

Introduction

Respiratory syncytial virus (RSV) is a single-stranded RNA virus of the para-myxoviridae family. RSV causes respiratory tract disease such as infections of the airways, lungs and middle ear. RSV is transmissible by sneezing and coughing or physical contacts such as kissing, touching or shaking hands. Unlike other cold viruses, RSV can survive up to 6-7 hours on objects and surfaces. Viral shedding persists for about 8 days, but can be significantly prolonged in immunocompromised individuals. RSV infection does not convey persistent immunity against future infections, even in the presence of significant antibody titres; however, higher titres may attenuate the course of the disease. RSV spreads very quickly in crowded households and daycare centres and is the most common cause of lower respiratory tract diseases among infants; virtually all children have been infected with RSV by 2 years of age, with nearly half having experienced two infections. The World Health Organization recently estimated that RSV accounts for more than 80% of acute lower respiratory tract infections in infants below 12 months old.¹

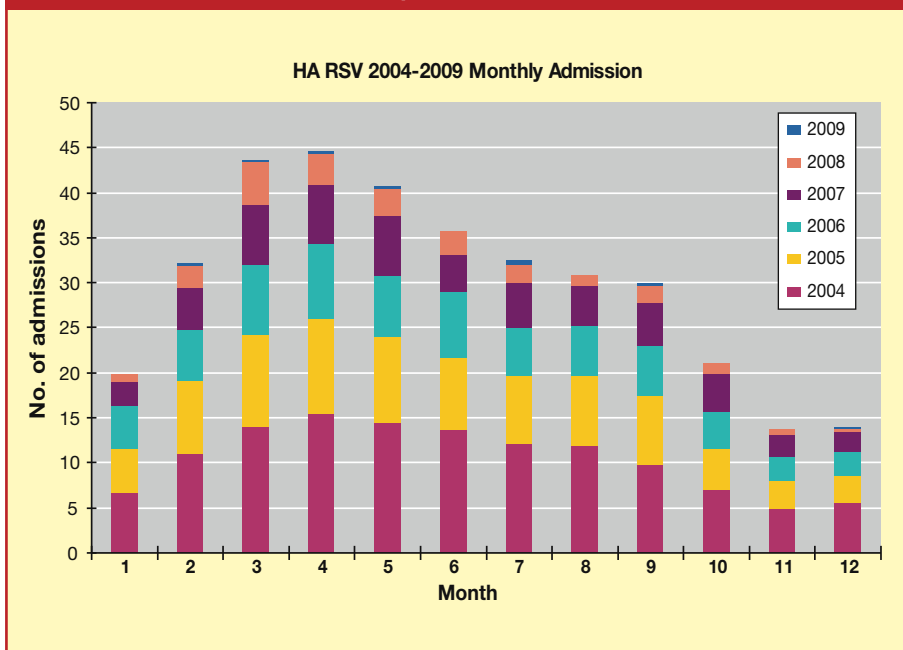
Most people with RSV suffer moderate to severe cold-like symptoms, but RSV infections can be more serious in high-risk infants. For example, RSV frequently leads to hospitalization or serious lung infections in babies born prematurely or with a heart or lung condition. RSV infection provokes an extremely complex inflammatory response that involves the release of multiple cytokines and chemokines from the epithelium and immunocytes, as well as mast cell degradations that release leucotrienes. RSV bronchiolitis may be

associated with short-term or long-term complications that include recurrent wheezing, reactive airway disease, and pulmonary function abnormalities. In the USA, it is estimated that as many as 126,000 infants per year (24.2 per 1,000) are hospitalized due to acute bronchiolitis, with 2–5 % requiring mechanical ventilation.² RSV infections kill up to 400 infants annually – a death rate 10 times higher than that of influenza.³

RSV Infections in Infants: Epidemiology and Disease Burden

In the USA and throughout the Northern Hemisphere, annual RSV epidemics usually begin in November, peak in January or February and end in May. RSV seasonality in Hong Kong is less predictable, and the disease remains active for nearly 10 months of the year. A local retrospective study showed that the season usually starts in April, peaks in July and August, and wanes in September, with monthly incidence strongly correlating with temperature and relative humidity.⁴ Based on Hospital Authority Clinical Discharge Information, this trend has become even more unpredictable in recent years, with outbreaks occurring even during the “off peak” season like November to January. (Figure) A local prospective population-based survey conducted from 2003 to 2006 showed very high rates of RSV hospitalization in infants less than 6 months old, with an incidence of 2.3–3.1 per 1,000. The mean duration of hospitalization associated with RSV infection was 4.04 days, which was substantially higher than that of influenza A and B, adenovirus and para-influenza.⁵

Figure. Monthly RSV admissions in Hospital Authority institutions



Clinical Manifestations and Diagnosis of RSV Infection

Infants with RSV infections typically present with upper respiratory symptoms, such as congestion and rhinorrhoea for 2–4 days, that progress to involve the lower respiratory tract and manifest as coughing, wheezing and laboured breathing. The severity of respiratory distress can vary from mild to profound life-threatening respiratory failure. Infants may also develop lethargy, poor feeding and fever resulting in dehydration. Apnoea is a well-known complication of RSV infection in young infants and may occasionally be severe enough to cause death.

RSV is diagnosed based on the clinical presentation and physical findings of diffuse polyphonic wheezing and coarse rales. Chest radiography shows bilateral hyperinflation, patch atelectasis, peribronchial thickening and interstitial infiltrates suggestive of pneumonic complications. Virological diagnosis can be made by direct immunofluorescent detection of RSV antigens in nasopharyngeal swabs or aspirates. Commercially available kits for detecting RSV antigen allow rapid diagnosis in the clinic setting, with a sensitivity of 80–95%. Definitive diagnosis

requires observation of a four-fold rise in RSV-specific immunoglobulin-G (IgG) titre.

Management

The mainstay of treatment for RSV infections is supportive care, with the intention of ensuring adequate oxygenation, improving respiratory secretion clearance, and meeting fluid and nutrition needs. Hospital admission for more aggressive management and monitoring might be needed for infants who are less than 3 months old or have pre-existing risk factors, difficulty feeding, pronounced respiratory distress, or require supplementary oxygen. Most infants with less severe disease can be managed as outpatients. Young infants are obligatory nasal breathers, and nasal congestion may result in significantly greater respiratory and feeding difficulties. Relief of nasal obstruction by simple nasal cleaning with saline drops and frequent suctioning with a home-used nasal aspirator are important measures. Small, frequent feeds can help to maintain hydration and prevent vomiting, which would increase the risk of aspiration. Although chest physiotherapy was once believed to help to mobilize secretions and recruit atelectatic lung, a recent Cochrane review found no evidence for such benefits.⁶ Indeed,

excessively vigorous physiotherapy may cause harm by inducing vomiting and precipitating apnoea in young infants.

Although medications are frequently used in infants suffering from RSV infections, most were not found effective and may be associated with significant side effects, especially in young infants. Routine use of bronchodilators such as beta-agonists, ephedrine and anticholinergic agents is controversial, and most randomized controlled trials found no objective evidence of clinical benefit.⁷ It is generally accepted that a trial of nebulized epinephrine or ipratropium bromide, either alone or combined with a beta-agonist, can be used in outpatient settings to assess the response in selected infants with severe wheezing. Some studies have suggested that there may be minor improvement in oxygenation, but there was no significant benefit on the overall clinical course. Systemic bronchodilators are not recommended because of their systemic side effects in young infants and the risk of fatal complications, especially for those with underlying cardiac problems.

Inhaled or systemic steroids were not found to reverse airway obstruction due to virally-induced wheezing in non-atopic young infants. Current evidence does not favour routine use of inhaled or systemic steroids, except in specific patients such as those with a strong family history of parental atopy or asthma, or a medical history (atopic eczema) consistent with atopic predisposition. A recent review showed that hypertonic saline (3%) nebulization can shorten the length of hospital stay by 25%,⁸ which probably relates to its beneficial effect in improving the mucociliary clearance of secretions. Many infants with RSV bronchiolitis are treated with antibiotics, especially if they have persistent fever. In fact, the risk of bacterial superinfections in the chest associated with RSV is quite low, except in infants who require intubation and ventilation. The most common secondary bacterial infections are those of the urinary tract (related to dehydration), or otitis media due to severe nasal obstruction and tubal blockage. In infants with persistent fever, or relapse of high fever, appropriate investigations should be performed to identify the site of sec-

ondary infection; antibiotics should be used to treat these secondary infections accordingly. Ribavirin is the only antiviral agent licensed to treat RSV; however, its routine use is limited due to inconclusive clinical benefits. Moreover, it is expensive, troublesome to administer, and is potentially teratogenic to exposed personnel. For these reasons, ribavirin should be restricted to treating selected immunocompromised patients, and is usually combined with anti-RSV antibodies to limit continued viral shedding.⁹

Immunoprophylaxis

Palivizumab is a humanized monoclonal IgG1 antibody produced by recombinant DNA technology. It has advantages over RSV-IVIg hyperimmune polyclonal globulin in terms of minimal immunosuppressive effect and no risk of transmitting blood-borne infection. Palivizumab can be easily administered by intramuscular injection in an outpatient setting. The American Academy of Pediatrics (AAP) recommends RSV prophylaxis with monthly intramuscular injections of palivizumab (15 mg/kg) during the RSV season for the following high-risk infants¹⁰:

1. Infants and children younger than 24 months old with chronic lung disease of prematurity who are receiving medical therapy within 6 months before the next RSV season begins.
2. Infants born before 32 weeks of gestation, even if they do not have chronic lung disease.
3. Infants born between 32 weeks to 34 weeks and 6 days of gestation, with at least one of the following two risk factors:
 - The infant attends child care, or
 - Has at least one sibling or another child younger than 5 years old who permanently resides in the same household.
4. Infants less than 1 year old with congenital abnormalities of the airway, or neuromuscular disease.
5. Infants and children up to 24 months old with haemodynamically significant congenital heart disease.
6. Infants with severe immunocompromise.

Palivizumab for RSV Prophylaxis for At-risk Infants – Local Perspective

Despite its clinically proven benefits, palivizumab is not widely used in Hong Kong due to its prohibitively high cost. The lack of clear RSV seasonality in Hong Kong also makes it more complicated to adopt recommendations similar to those of the AAP for local high-risk infants. Due to lack of local epidemiological and pharmaco-economic data supporting its cost-effectiveness, public hospitals do not offer palivizumab to eligible at-risk infants. Very few private paediatricians systematically provide information on RSV immunoprophylaxis to parents of at-risk infants. Based on AAP recommendations, the author has been providing counselling and information leaflets on RSV prevention and prophylaxis to parents of at-risk infants shortly discharged from hospital. During the past 3 years (2009–2011), 24 eligible infants were treated with palivizumab immunoprophylaxis. All but two were extremely premature babies born from 24 weeks to 32 weeks gestation (mean, 28.1 weeks) who had chronic lung disease, and five were oxygen-dependent at hospital discharge. One of the other two infants suffered from congenital heart disease with congestive heart failure, and the other had a rare syndromal disorder, with oxygen-dependent chronic lung disease and severe upper airway obstruction. Most of these infants received one course of three to six doses at monthly intervals during the first 3–6 months post discharge from hospital, coinciding with the peak RSV season in Hong Kong (mostly March to August). The number of doses given was titrated based on the prevalence of RSV and the severity of the underlying lung condition, in order to maximize the cost-effectiveness of treatment. Two infants (a 25-week premature baby and the one with syndromal disorder, who both remained oxygen-dependent in the second RSV season) received two courses of five doses of palivizumab in two consecutive peak RSV seasons. None of the treated infants required hospitalization for respiratory tract infection during the treatment period, and only one suffered from an RSV infection; this infant recovered promptly

with conservative management. This small series suggests that palivizumab is effective in preventing and reducing the morbidity of RSV infection in at-risk infants.

Recently, The Hong Kong Society of Paediatric Respiriology convened a panel of leading Hong Kong paediatricians, neonatologists, microbiologists and respiratoryologists to discuss the impact of RSV infection and its management in the local paediatric population. The panel suggested that in the absence of local epidemiological and pharmaco-economic data and given limited experience in the use of palivizumab locally, recommendations on immunoprophylaxis should be limited to the highest-risk individuals to ensure its cost-effectiveness. While government funding is not currently available to provide support for its use, parents of at-risk infants should be given adequate information so that they are in a better position to balance the benefit and affordability. Local recommendations should help paediatricians to identify patients at risk, and in such cases they are obliged to inform the parents of the option of immunoprophylaxis. It is important for physicians to endeavour to maximize the treatment benefits according to their patients' ability to pay.

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Rheumatoid Arthritis: Advances in Therapeutics



Dr Cheung Tak Cheong
(張德昌醫生)

MBBS, MRCP, PDipID, FHKCP, FHKAM, FRCPE

Specialist in Rheumatology

Private Practice

Key words:

Biologics (生物製劑),
rheumatoid arthritis (類風濕關節炎),
treatment (治療)

Introduction

Undertreated rheumatoid arthritis (RA) can cause functional impairment, deformity and early death. However, through early and aggressive intervention, it is now possible to halt and prevent the accumulation of permanent joint damage. Greater understanding of the pathogenesis of RA has resulted in recent advances in its treatment. This article reviews experience in the management of RA gained with tumour necrosis factor (TNF) inhibitors and also discusses newer biological agents and other targeted small molecules that act on signalling pathways. All of these modalities are expanding our knowledge of RA and providing more effective and efficient treatment options.

First-generation Biologics: TNF Inhibitors

Efficacy in RA

The development of biologic agents that selectively block cytokines has been a major advance in the treatment of RA. TNF is a proinflammatory cytokine abundant in patients with RA.¹ Currently, three TNF-targeting agents dominate the biological management of RA: Etanercept, a dimeric fusion protein, consists of the extracellular portion of human p75 TNF receptor linked to the Fc region of human immunoglobulin-G1. Infliximab is a chimeric human/mouse monoclonal antibody comprising the human constant and murine variable regions. Adalimumab is a recombinant human monoclonal antibody specific to TNF. All three anti-TNF therapies have well-demonstrated efficacy in RA.

Any of these TNF inhibitors may be given concomitantly with methotrexate (MTX) therapy; randomized controlled

trials showed that combinations with MTX are significantly more effective than MTX alone in achieving disease remission, reducing signs and symptoms of RA, slowing or stopping radiographic progression of disease and improving physical function. Although TNF inhibitors are currently the recommended first-line biological agents for patients with RA, there are several unanswered questions about how to derive the maximum benefit from such agents. Convincing data indicate that using biologics early in the course of RA can be highly efficacious and may induce clinical remission.²⁻⁶ Family physicians and other healthcare professionals must be educated about the early symptoms of RA, with an emphasis on the importance of early referral to rheumatologists for diagnosis and treatment.

Potential for Effectiveness of TNF Antagonists in Early RA

The PREMIER study compared the efficacy of early intervention with combined adalimumab and MTX vs either agent as monotherapy in patients with early, aggressive RA.³ The primary endpoints in this 2-year, double-blind, controlled study were the percentage of patients in whom an American College of Rheumatology 50% (ACR50) response was achieved and the mean change from baseline in the modified Total Sharp Score (TSS), which assesses bone erosion and joint space narrowing on radiographs. Adalimumab and MTX combination therapy was superior to monotherapy for all outcomes measured. At 1 year, patients treated with combination therapy had a mean increase in TSS of 1.3 units compared with 3.0 units in those receiving only adalimumab and 5.7 units in the MTX monotherapy arm. At 2 years, patients receiving combination therapy continued to have significantly less radiographic progression (mean change 1.9 TSS units) compared with those treated with either adalimumab (5.5 units) or MTX (10.4 units)

monotherapy. Although ACR responses were comparable in the two monotherapy arms, there was significantly less progression in the adalimumab arm than the MTX arm at 6 months (2.1 vs 3.5), 1 year (3.0 vs 5.7) and 2 years (5.5 vs 10.4). These results suggest that combination therapy in early RA is beneficial.

Furthermore, drug-free remission may be a realistic goal in some patients with early RA. In the BeSt study, 19% of patients who received infliximab plus MTX in a Disease Activity Status (DAS)-steered, tightly controlled manner were in drug-free remission at 5 years, for a mean duration of 22 months. Infliximab was successfully discontinued in 58% of patients, while 18% were still receiving combination therapy. Moreover, compared with other treatment strategies, initial temporary treatment with infliximab plus MTX resulted in significantly better functional ability over 5 years.⁷ This study raises the possibility that if aggressive treatment to induce remission is instituted very early in the course of RA, more conservative management strategies may be sufficient to maintain that remission.

“Drug-free remission may be a realistic goal in some patients with early RA”

Safety

Bacterial infections, including sepsis and pneumonia, invasive fungal infections, and other opportunistic infections have all been associated with the use of TNF inhibitors. Reactivation of latent tuberculosis following treatment has led to the introduction of preinitiation screening procedures, which have successfully reduced the number of reported cases.^{8,9} The risk of reactivating latent tuberculosis depends on the incidence of latent infection and is associated with all TNF inhibitors. Physicians should remain alert to the development of symptoms related to tuberculosis or other infections. Patients with congestive heart failure should be closely monitored. Other rarely reported conditions that are possibly related to use

of TNF inhibitors include demyelinating diseases, seizures, aplastic anaemia, pancytopenia, and drug-induced lupus. Physicians should remain vigilant for the development of such conditions.

Advances in Biological Therapy

The pathogenesis of RA is a highly complex interplay of numerous inflammatory pathways.¹⁰ Many biological agents that intervene in various pathways have potential, or are being developed, to treat RA.

Rituximab

Rituximab is a chimeric anti-CD20 monoclonal antibody that was the first B-cell agent approved for treating RA.¹¹ Rituximab inhibits progression of structural damage in RA over 2 years, and long-term treatment continues to inhibit joint damage.^{12,13} A prospective cohort study found that patients who were switched to rituximab due to TNF inhibitor ineffectiveness had significantly better disease improvement than those treated with an alternative TNF inhibitor.¹⁴ Progressive multifocal leukoencephalopathy or hepatitis B reactivation both occur very rarely during rituximab treatment.

Abatacept

Abatacept is a T-cell co-stimulation modulator that is believed to prevent the activation of T lymphocytes, including naïve T cells. Because abatacept was the first therapy targeting the inhibition of co-stimulatory signals to prevent T-cell activation, its use in early disease and in biologic-naïve patients with active RA has generated particular interest and research.^{15,16} Abatacept has also been shown to provide clinical benefits in patients with RA who failed earlier TNF inhibitor treatment, regardless of which TNF inhibitors were used or the reasons for treatment failure.¹⁷ This finding suggests that switching to abatacept may be a useful option for patients who fail TNF inhibitor treatment.

Tocilizumab

Tocilizumab is a humanized anti-

interleukin-6 (IL-6) receptor monoclonal antibody that inhibits signals through both membrane and soluble IL-6 receptors. Data from four randomized, double-blind, controlled, phase III trials of tocilizumab in different populations support its use in RA, including patients refractory to MTX or other disease-modifying anti-rheumatic drugs (DMARDs) (OPTION, TOWARD, LITHE),¹⁸⁻²⁰ and MTX-naïve patients (AMBITION).²¹ Compared with placebo in these trials, tocilizumab significantly improved ACR 20% response (ACR20), physical function, fatigue, and physical and mental health scores over 24 weeks. In the 3-year extension of the SAMURAI study, radiographic progression was strongly suppressed in patients with early RA who were treated with tocilizumab.²² Furthermore, radiographic progression was more effectively suppressed in patients who received initial treatment with tocilizumab compared with conventional DMARDs. Early introduction of tocilizumab treatment may therefore be more effective in preventing joint damage. Tocilizumab has a well-characterized safety profile, with infections being the most common adverse event. Physicians should also check for decreased neutrophil counts and increased lipid or liver enzyme levels, and manage these appropriately.

Kinase Targets in Development

Kinases such as Janus kinase (JAK) are intracellular molecules that play a pivotal role in signal transduction of interleukins. Tofacitinib is a pan-JAK inhibitor that inhibits JAK1 and JAK3 to a greater extent than JAK2, and is effective in patients who respond inadequately to DMARDs. In a phase III trial, patients treated with tofacitinib 10 mg twice-daily had a significantly better ACR20 response than placebo (65.7% vs 26.7%).²³

Also of interest are data indicating that spleen tyrosine kinase could serve as a new and promising target for immune intervention in rheumatic diseases. In a phase II study of RA patients refractory to MTX, more of those treated with fostamatinib, which is a potent spleen tyrosine kinase inhibitor, than in the placebo group attained an ACR20 response at week 12 (67% vs 35%).²⁴

Conclusion

Biological therapies have revolutionized the treatment of RA and allowed us to further curb its progression. Development of the first biologics, TNF inhibitors, expanded our knowledge of the pathogenesis of inflammatory conditions. A large body of safety and efficacy data on TNF inhibitors has accumulated during more than a decade that they have been available to rheumatologists. More recently, biologics with distinct mechanisms of action (rituximab, abatacept, tocilizumab) have been approved. Numerous other targets within the inflammatory cascade continue to be identified, and biologic and nonbiologic agents to modulate/inhibit the associated pathways have already been developed, or are in the pipeline.

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The Challenge and Essence of the Management of Psoriasis



Dr Hui Shiu Kee (許紹基醫生)

LMCHK, MRCP (UK), FHKCP, FHKAM
(Medicine)

Specialist in Dermatology and
Venereology,
Private Practice

Key words:

Psoriasis (牛皮癬), management (治理),
biologics (生物製劑)

Psoriasis is a cutaneous and systemic chronic inflammatory disorder that results from both internal genetic factors (polygenic abnormalities) and external environmental factors (trauma, infection and medications). It is relatively common in Western countries, with a prevalence of 2%, while the prevalence ranges from 0.3–1.1% in Asian and African countries.¹

Although the prevalence of psoriasis is not as high as that of atopic

eczema, psoriasis has significant negative impact on the everyday life of a patient. Moreover, up to 40% of patients with psoriasis regard the treatment they received as unsatisfactory. The management of psoriasis remains a challenge in routine clinical practice of general physicians and dermatologists alike. This article will discuss the essence of managing this challenging disease under four headings: I) General management; II) specific therapy; III) the challenges for patients; and IV) the challenges faced by physicians. The management of specific types of psoriasis such as palmoplantar pustulosis, pustular psoriasis and erythrodermic psoriasis are not discussed in this article.

General Management of Psoriasis

While taking detailed medical history, some points are important and worth mentioning to the patients.

The positive side of the nature of this illness should be stressed. It is important to point out that psoriasis is not contagious, and the family and friends will not be “infected”. It is also constructive to point out that up to 40% of patients may enjoy a period of remission that may last for up to 54 years.² During that period, patients will be free of any signs and symptoms of psoriasis even without any treatment. Finally, the fact that an increasing number of effective agents such as biologics will become available proposes a brighter future for psoriatic patients.³ The confidence gained by patients will largely improve their treatment compliance, which in turn will improve the effectiveness of treatment.

A realistic picture of the level of control with different treatment measures, and their potential long-term risk and implications, especially the long-term side effects and financial expenditure, should all be communicated to patients for their thorough consideration.

Patients’ own perception of the illness and their expectation of treatment outcome should be understood by the attending physician before asking for commitment to a long-term treatment plan. This approach will largely eliminate the unnecessary iatrogenic damage from the

physician and unrealistic expectations from the patients.

General Advice on Lifestyle Adjustment

Since psychological stress is a well-known predisposing factor of psoriasis,⁴ simple general measures that enhance the sense of well-being might help enormously and should be encouraged. These include applying moisturizers properly, adequate rest, abstinence from smoking and drinking,⁵ taking good wound care and refraining from excessive scratching of skin, gradual arrangement for sun exposure, and participating in self-help support groups and health talks on psoriasis.

Eliminating Infection

Upper respiratory tract infections and urinary tract infections are considered as predisposing factors for psoriasis. Patients should be encouraged to seek early medical advice if they have warning symptoms.

Medications

Medications known to exacerbate psoriasis, such as lithium and beta-blockers, should be discontinued.⁶

Specific Therapy of Psoriasis

The selection of specific therapies for patients with psoriasis should be based on all the aforementioned factors, such

as patients’ general physical condition, social economic status, expectation of treatment outcome, perception of the impact of psoriasis, current disease activity and clinical variants of psoriasis. Four major therapeutic approaches can then be considered, namely topical therapy, phototherapy, systemic therapy and biologic therapy.

The pros and cons of these four approaches are summarized in the Table.

Medications and treatment modalities commonly used in Hong Kong are listed below:

Topical Therapy

Vitamin D3 analogues (calcipotriol [Daivonex], calcitriol [Silkis]) are effective in localized psoriasis, but local irritation may occur on the face and intertriginous area.

Topical corticosteroids are the mainstay of treatment for small lesions of psoriasis (<5% body surface area). Tachyphylaxis can be reduced if the duration of continuous treatment is restricted to less than 2 weeks and switched to weekend application only.

Topical calcineurins (tacrolimus [Protopic], pimecrolimus [Elidel]) are useful for treatment of facial and flexural psoriasis, since these areas are prone to corticosteroid side effects and irritation from vitamin D analogues.

Coal tar is effective but messy. Salicylic acid is keratolytic and can remove scaly plaques. It inactivates calcipotriol and blocks UVB, and should therefore be avoided in the presence of the above therapies. Tararotene and anthralin have

Table. Pros and cons of therapeutic approaches for psoriasis

	Pros	Cons
Topical therapy	<ul style="list-style-type: none"> Convenient, economic Relatively free from systemic side effects Predictable effect on patients with less than 5% body surface area involvement Self-administered 	<ul style="list-style-type: none"> Have no effect on reducing the occurrence of new lesions Long-term usage should be under medical supervision; otherwise there will be problems of tolerance and/or tachyphylaxis
Phototherapy	<ul style="list-style-type: none"> Relatively safe and free of systemic side effects Good for widespread disease May have prompt improvement after a few treatment sessions 	<ul style="list-style-type: none"> Time-consuming Facility-dependent Expenses may be a concern Not suitable for physically compromised patients
Systemic therapy	<ul style="list-style-type: none"> Convenient Suitable for widespread disease Some with relatively prompt improvement 	<ul style="list-style-type: none"> Systemic side effects common after long-term usage Regular laboratory monitoring needed in some patients Many patients may have pre-existing medical conditions that are relative or absolute contraindications
Biologic therapy	<ul style="list-style-type: none"> Good response Relatively free of systemic side effects Some are relatively convenient 	<ul style="list-style-type: none"> Very expensive Relative short history of clinical usage, awaiting long-term established safety profile Some have potential risk of exacerbating infection

problems of skin irritation and are less commonly used.

Phototherapy

Narrow band ultraviolet B (nUVB) and photochemotherapy with psoralen and ultraviolet A (PUVA) are used relatively commonly in Hong Kong. Targeted phototherapies with Excimer (308 nm) laser or lamp are more effective for localized lesions, but only available in a few centres.

Systemic Therapy

Methotrexate, cyclosporine and acitretin are the three major systemic agents used in the management of psoriasis.

Methotrexate is effective, economic and has relatively prompt disease control. However, hepatotoxicity and marrow suppression with idiosyncratic reaction are its major drawbacks.

Cyclosporine is also effective and has prompt disease control. However, it is relatively expensive, and nephrotoxicity and hypertension are its common side effects, limiting its use to less than 1 to 2 years. Acitretin is relatively safe in terms of organ toxicity, with reversible mild-to-moderate alterations in liver enzymes and blood lipids. It takes approximately 2 weeks to have noticeable effect on disease progress.

Biologic Therapy

Currently available biologics for treatment of psoriasis include the tumour necrosis factor (TNF) inhibitors infliximab (Remicade), etanercept (Enbrel) and adalimumab (Humira), the interleukin-12/interleukin-23 inhibitor ustekinumab (Stelara), and the T-cell inhibitor alefacept (Amevive). All of these new agents are expensive but effective for the treatment of psoriasis. Approximately 60–70% of patients using these agents will have 75% improvement of psoriasis in 2 to 3 months. The major concern with this approach might be treatment cost and their unknown long-term safety profile.⁷⁻¹¹

Challenge for Patients With Psoriasis

Misconception of the Public

Historically, patients with psoriasis had

suffered from unjustified discrimination for centuries due to the visible lesions of psoriatic plaques. Even though Robert Wilan and Hebra recognized psoriasis as a distinct entity from leprosy in the first half of the 19th century, public understanding of the noncontagious nature of this illness seems far from adequate, making it a heavy psychological burden for psoriatic patients. Proper education of the public will ease this burden, making life easier for psoriatic patients.

Unrealistic Expectations

Patients may have unrealistic expectations of cure towards some new approaches and newly encountered physicians. However, after a certain period of remission and recurrence, confidence and compliance deteriorate due to less satisfactory psoriasis control, and patients become over-pessimistic towards any other potentially effective therapeutic approaches, resulting in further deterioration of psoriasis, even into erythrodermic stage.

“Look for well-circumscribed cutaneous lesions, scaling lesions under hair, pitting nails and family history of unknown dermatoses”

Challenge for Physicians

Diagnostic Problems

It is not uncommon for an experienced dermatologist to make a definite diagnosis of psoriasis after years of treating the same patient labeled with chronic eczema. Vigilantly looking for well-circumscribed cutaneous lesions, scaling lesions under hair, pitting nails and family history of unknown dermatoses may help

reveal the real picture. Adequate consultation time with suitable sampling of skin biopsy in difficult cases is valuable, since topical and systemic steroids may dramatically alter the clinical as well as histological presentation of the illness.

Patients' Compliance

Patients' compliance is the key to good disease control. Patients' trust builds on robust communication with the attending physician. The more knowledgeable the patients are on psoriasis, the more willing will they be to act according to the treatment plan, which should be tailored for their long-term betterment and short-term needs.

The expected time to have noticeable improvement of psoriasis from different therapies should be told beforehand. Patients should be encouraged to report any unwanted or unexpected experience with treatment and they should be promptly explained and/or resolved.

While patients accept the no-cure reality of psoriasis, sensible and pragmatic approaches in controlling the symptoms and signs of psoriasis would be appealing.

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Role of Chemotherapy in Soft Tissue Sarcoma



Dr Loh Kai Tsu, Kevin
(陸凱祖醫生)

FACP, FRCPC

Specialist in Medical Oncology,
Private Practice

Key words:

Chemotherapy (化療), soft tissue sarcoma (軟組織肉瘤), trabectedin

Table. Chemotherapy agents and regimens with activity in soft tissue sarcoma	
Sarcoma type	Chemotherapy agents and regimens
General	<ul style="list-style-type: none"> • Doxorubicin monotherapy • Doxorubicin, ifosfamide and mesna (AIM) • Doxorubicin and dacarbazine (AD) • Mesna, doxorubicin, ifosfamide and decarbazine (MAID) • Epirubicin, ifosfamide and mesna • Gemcitabine and docetaxel • Gemcitabine and vinorelbine
Leiomyosarcoma	<ul style="list-style-type: none"> • Doxorubicin, gemcitabine, dacarbazine • Gemcitabine and docetaxel
Myxoid liposarcoma	<ul style="list-style-type: none"> • Anthracyclines • Trabectedin • Ifosfamide
Synovial sarcoma	<ul style="list-style-type: none"> • Anthracyclines • Trabectedin • Ifosfamide
Poorly-differentiated liposarcoma	<ul style="list-style-type: none"> • Ifosfamide
Angiosarcoma	<ul style="list-style-type: none"> • Paclitaxel or docetaxel • Liposomal doxorubicin • Sorafenib
Desmoid tumours (fibromatosis)	<ul style="list-style-type: none"> • Doxorubicin-based regimens • Hormonal therapy (eg, tamoxifen ± sulindac) • Methotrexate and vinblastine

Adapted from reference 1.

Sarcomas are a heterogeneous group of mesenchymal neoplasms that can be grouped into two general categories: soft tissue sarcomas (STS) and bone sarcoma. Bone sarcomas (osteogenic sarcoma and Ewing’s sarcoma) are considered chemotherapy sensitive, but STS are generally more resistant to chemotherapy.¹ This review summarizes the emerging role of systemic chemotherapy in STS.

At diagnosis, fewer than 50% of patients with STS will be prescribed curative treatment with surgery or radiation therapy. However, 30–60% of patients with clinically localized disease at presentation will eventually develop local recurrence or metastases, mostly in the lungs. Metastatic STS is usually not amenable to curative treatment, and palliation with systemic therapy remains an urgent clinical problem.

Chemotherapy in Metastatic STS

Appropriate use of chemotherapy may be of some benefit in treating metastatic STS. Experience shows that certain patients tend to respond better to chemotherapy, including: those who are young; have good performance status; without liver involvement; and long disease-free interval between primary surgery and relapse. Single-agent doxorubicin, ifosfamide or dacarbazine, or anthracycline-based combination regimens (eg, doxorubicin or epirubicin with ifosfamide and/or dacarbazine) produce objective responses in 13–33% of patients, but do not usually improve overall survival. More recently, gemcitabine and taxane combinations have demonstrated activity in STS, especially in leiomyosarcoma.²

Certain histologic subtypes such as GIST, alveolar soft part sarcoma, clear cell sarcoma, well-differentiated liposarcoma are intrinsically resistant to chemotherapy. In contrast, leiomyosarcoma, myxoid and poorly-differentiated liposarcoma, angiosarcoma and synovial sarcoma are more sensitive to chemotherapy. The Table lists the choice of chemotherapy agents for various sarcoma histologies.¹

systemic chemotherapy in STS is unproven. Although several meta-analyses have shown that modern adjuvant chemotherapy can improve disease recurrence rate and increase disease free survival,³ there is usually no increase in long-term overall survival. The choice of adjuvant chemotherapy should conform to the same agents that perform best in the metastatic setting.

Preliminary trials showed that trabectedin has substantial activity in STS, particularly among leiomyosarcomas and myxoid liposarcomas, with response rates up to 51% and prolonged disease control.⁴ Toxicity is limited to transient reversible liver enzyme elevation and myelosuppression. Trabectedin and anthracycline combinations are now being used in STS and ovarian carcinoma.

Chemotherapy in the Adjuvant Setting

Patients with higher grade, deep seated and larger (>5 cm) STS are more prone (>50%) to local recurrence and metastases, despite surgery and local radiation therapy. The role of adjuvant

Trabectedin – a New Chemotherapy Agent in STS

Trabectedin (ET-743), which was derived from a marine tunicate, is a new chemotherapeutic agent that induces deoxyribonucleic acid double-strand breaks.

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Specialist in Endocrinology, Diabetes and Metabolism
- 1:00 pm – 2:00 pm ※※※※※ **Lunch** ※※※※※
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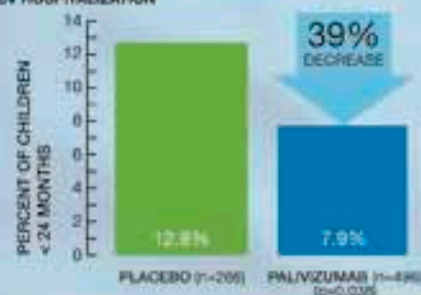
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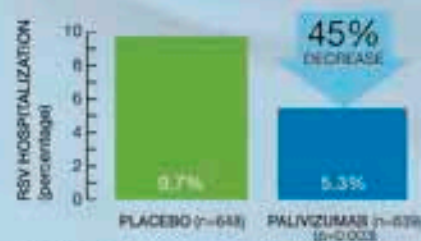
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